

WHAT IS CLAIMED IS:

1 1. An isolated nucleic acid encoding a peptide consisting of about 21 to 40
2 amino acids comprising a ZA loop of a bromodomain comprising the amino acid
3 sequence of SEQ ID NO:3.

1 2. The isolated nucleic acid of Claim 1 further comprising a heterologous
2 nucleotide sequence.

1 3. An isolated nucleic acid encoding a peptide consisting of about 21 to 40
2 amino acids comprising a ZA loop of a bromodomain, wherein the bromodomain has
3 an amino acid sequence selected from the group consisting of SEQ ID NOs. 7, 8, 9,
4 10, 11, 12, 13, 14, 15, 16, 17, 18, 19, 20, 21, 22, 23, 24, 25, 26, 27, 28, 29, 30, 31, 32,
5 33, 34, 35, 36 , 37, 38, 39, 40, 41, and 42.

1 4. The isolated nucleic acid of Claim 3 further comprising a heterologous
2 nucleotide sequence.

1 5. A peptide consisting of about 21 to 40 amino acids comprising a ZA loop of
2 a bromodomain comprising the amino acid sequence of SEQ ID NO:3.

1 6. A fusion protein or peptide comprising the peptide of Claim 5.

1 7. A peptide consisting of about 21 to 40 amino acids comprising a ZA loop of
2 a bromodomain, wherein the bromodomain has an amino acid sequence selected from
3 the group consisting of SEQ ID NOs. 7, 8, 9, 10, 11, 12, 13, 14, 15, 16, 17, 18, 19, 20,
4 21, 22, 23, 24, 25, 26, 27, 28, 29, 30, 31, 32, 33, 34, 35, 36 , 37, 38, 39, 40, 41, and
5 42.

1 8. A fusion protein or peptide comprising the peptide of Claim 7.

1 9. An antibody raised against the peptide of Claim 7 or raised against an
2 antigenic fragment thereof.

1 10. An antibody raised against the peptide of Claim 5.

1 11. A method of identifying a compound that modulates the affinity of a
2 bromodomain for a ligand that comprises an acetyl-lysine,
3 said method comprising:

4 (a) contacting the bromodomain and the ligand in the presence of the
5 compound, wherein the bromodomain and the ligand bind in the absence of the
6 compound; and

7 (b) measuring the affinity of the bromodomain for the ligand; wherein
8 a compound is identified as a compound that modulates the affinity of the
9 bromodomain for the ligand when there is a change in the affinity of the
10 bromodomain for the ligand in the presence of the compound.

1 12. The method of Claim 11, wherein the affinity of the bromodomain for the
2 ligand increases in the presence of the compound and wherein the compound is
3 identified as a bromodomain-ligand complex promoting agent.

1 13. The method of Claim 11, wherein the affinity of the bromodomain for the
2 ligand decreases in the presence of the compound and the compound is identified as an
3 inhibitor.

1 14. The method of Claim 11, wherein the compound is selected by performing
2 rational drug design with the set of atomic coordinates obtained from one or more of

3 Tables 1-6, wherein said selecting is performed in conjunction with computer
4 modeling.

1 15. The method of Claim 11, wherein the compound is selected by performing
2 rational drug design with the set of atomic coordinates obtained from a set of atomic
3 coordinates defining the three-dimensional structure of a bromodomain consisting of
4 the amino acid sequence of SEQ ID NO:7, wherein said selecting is performed in
5 conjunction with computer modeling.

1 16. A method of identifying a compound that modulates the stability of a
2 bromodomain-acetyl-lysine binding complex comprising:

3 (a) contacting the bromodomain-acetyl-lysine binding complex in the
4 presence of the compound wherein the bromodomain-acetyl-lysine binding complex
5 forms in the absence of the compound; and

6 (c) measuring the stability of the bromodomain-acetyl-lysine binding
7 complex; wherein a compound is identified as a compound that modulates the stability
8 of the bromodomain-acetyl-lysine binding complex, when there is a change in the
9 stability of the bromodomain-acetyl-lysine binding complex in the presence of the
10 compound.

1 17. The method of Claim 16, wherein the stability of the bromodomain-acetyl-
2 lysine binding complex increases in the presence of the compound and wherein the
3 compound is identified as a stabilizing agent.

1 18. The method of Claim 16, wherein the stability of the bromodomain-acetyl-
2 lysine binding complex decreases in the presence of the compound and the compound
3 is identified as an inhibitor.

1 19. The method of Claim 16, wherein the compound is selected by performing
2 rational drug design with the set of atomic coordinates obtained from one or more of
3 Tables 1-6, wherein said selecting is performed in conjunction with computer
4 modeling.

1 20. The method of Claim 16, wherein the compound is selected by performing
2 rational drug design with the set of atomic coordinates obtained from a set of atomic
3 coordinates defining the three-dimensional structure of a bromodomain consisting of
4 the amino acid sequence of SEQ ID NO:7, wherein said selecting is performed in
5 conjunction with computer modeling.

1 21. A method of identifying a binding partner for a protein that comprises an
2 acetyl-lysine said method comprising:

3 (a) contacting the protein with a polypeptide comprising a
4 bromodomain; and

5 (b) determining whether the polypeptide binds to the protein; wherein
6 a binding partner for a protein is identified when polypeptide binds to the protein.

1 22. The method of Claim 21 wherein the bromodomain has an amino acid
2 sequence from selected from the group consisting of SEQ ID NOS. 7, 8, 9, 10, 11, 12,
3 13, 14, 15, 16, 17, 18, 19, 20, 21, 22, 23, 24, 25, 26, 27, 28, 29, 30, 31, 32, 33, 34, 35,
4 36 , 37, 38, 39, 40, 41 and 42.

1 23. An agent that can inhibit the binding of a bromodomain with a protein
2 comprising an acetyl-lysine selected from the group consisting of : ISYGR-AcK-
3 KRRQRR (SEQ ID NO:4), ARKSTGG-AcK-APRKQL (SEQ ID NO:5) and
4 QSTSRHK-AcK-LMFKTE (SEQ ID NO:6).